REMARKS

Applicants thank the Examiner for allowing the subject matter of amended claims 51 and 52, and for pointing-out that the amended claims as filed on June 16, 2005 did not comply with current amendment practice as outlined by rule 1.121(c)(2).

This response is being submitted after receiving a second non-final Office Action mailed on July 20, 2005. This action reopened examination by citing a new basis for rejection. This second Action also made moot the Office's earlier final Office Action, According, the objection to claims 51 and 52 was withdrawn.

Pending claims 51 and 52 now stand rejected; claim 51 is rejected as obvious over Soonpaa *et al.*, in view of Li *et al.*, (newly cited art) and claim 52 over Soonpaa in view of Li *et al.*, and ENTREZ Nucleotide Database Entry Accession No. X68452 (newly cited art).

In response, Applicants have re-written claims 51 and 52 to each recite the phrase "An isolated cardiomyocyte cell". Applicants also submit and request consideration of for newly added claims 85-90 these claims all depend from claims 51 and 52. Accordingly, if claims 51 and 52 are allowable so too are the remaining claims all of which depend from claims 51 and 52. Soonpaa *et al.*, discloses expressing cyclin D1 in transgenic animals while amended claims 51 and 52 recite isolated cells. Accordingly, the amended claims are distinct from the disclosure of Soonpaa and it is improper to combine Soonpaa with either Li *et al.* or Li *et al.* and X68452 to assert that amended claims 51 and 52 are obvious over these references.

Li *et al.*, teaches that, "expression of cyclins D2 and D3 and of CDK4 and CDK6 increased significantly from day 3 to day 21 after AC concomitant with increased LV

mass". Abstract, Li *et al.* Li *et al.*, reports measuring an increase in cyclin D2 level in cardiomyocytes undergoing hypertrophic growth. Hypertrophic growth is undoubtedly accompanied by an increase in any number of cell proteins and protein activities. Li *et al.*, only report on the fate of a subset of proteins that undergo changes in expression level or activity during hypertrophic growth. Li, *et al.*, does not report that increasing the level of cyclin D2 in cardiomyocytes is responsible for an increase in hypertrophic growth. From reading Li *et al.*, it is no more obvious to express cyclin D2 to induce hypertrophic growth than it would be to induce the express levels of any of the other proteins whose levels increase during hypertrophic growth. In contrast, rather than reporting on changes that occur in cardiomyocytes undergoing proliferation data in the instant Application includes showing data that expressing cyclin D2 in cardiomyocytes promotes cardiomyocyte proliferation.

Li, *et al.* reports measuring changes in cardiomyocytes undergoing hypertrophic growth. Li, *et al.* does not report changes that accompany, much less cause an increase the proliferative potential of cardiomyocytes. Hypertrophic growth is defined as an increase in cell size. See Li, *et al.*, pg. 1, bridging col. 1-2. In contrast, the instant Application shows that increasing the expression of cyclin D2 increases the potential of cardiomyocytes to proliferate. Applicants teach that increasing the level of cyclin D2 increases the potential for cardiomyocytes to divide to form new cells thereby increasing the total number of cardiomyocyte cells. See Application, Example 7, page 32.

Hypertrophic growth and cell proliferation are clearly different metabolic process. The amended claims 51 and 52 of the Application recite that increasing the level of cyclin D2 in cardiomyocytes increases the proliferative potential of cardiomyocytes.

These claims are directed towards cardiomyocyte proliferation and are not obvious over the disclosure of Li, *et al.* which reports on some of the changes that cardiomyocytes undergo during hypertrophic growth. Accordingly, the claims of the Application are not obvious over Soonpaa in view of either Li, *et al.*, or combined with X X68452.

Li *et al.*, states that, "Future experiments designed to induce forced expression of these molecules in cardiomyocytes should offer an approach to determine the precise role of cell cycle regulatory molecules in cardiomyocyte hypertrophy and may lead to strategies for improving the prognosis of this disease". Li *et al.*, pg. H822. Again the disclosure of Li, et al., is directed to the study of the hypertrophic growth of cardiomyocytes and not to increasing the proliferative potential of cardiomyocytes. This passage taken with the rest of Li does not single out the importance of cyclin D2 in cardiomyocyte as Li *it al.* also discloses measuring many other changes that occur in cardiomyocyte cells during hypertropic growth. These changes include changes in the activities (and perhaps levels) of various kinases including CDK2, CDK4, and cyclin D3. See Li *et al.*, Figs. 4-5. In part, because, Li *et al.* teaches only changes measured in cardiomyocytes undergoing hypertrophic growth combining Li *et* al. with Soonpaa *et al.* does not make obvious expressing cyclin D2 in cardiomyocytes as a means of increasing the proliferative potential of cardiomyocytes. Accordingly, amended claims 51 and 52 are not obvious in view of the cited references.

In view of the foregoing, reconsideration and allowance of this Application, including amended claims 51, 52 and newly added claims 85-90 is requested.

The Examiner is invited to contact the undersigned attorney by telephone if there are any questions about this submission or other matters that may be readily addressed by telephone to expedite the allowance of this application.

Respectfully Submitted,

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